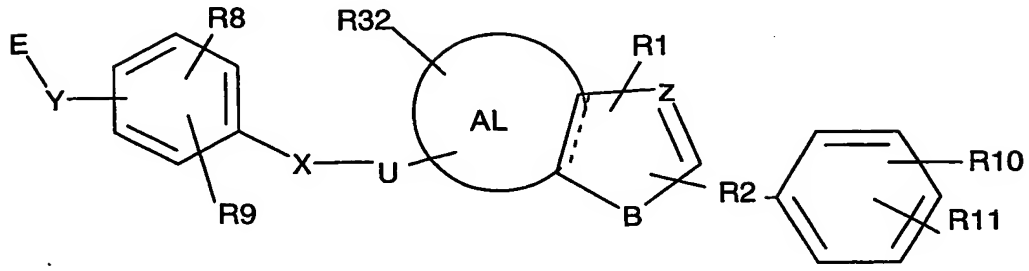
CLAIMS

What is claimed is:

1. A compound of the structural Formula I':



and stereoisomers, pharmaceutically acceptable salts, solvates and hydrates thereof, wherein:

(a) R1 is selected from the group consisting of hydrogen, C_1-C_8 alkyl, C_1-C_8 alkenyl, aryl-C_{0-4}-alkyl, aryl-C_{1-4}-heteroalkyl, heteroaryl-C_{0-4}-alkyl, C3-C6 cycloalkylaryl-C_{0-2}-alkyl, and, wherein C_1-C_8 alkyl, C_1-C_8 alkenyl, aryl-C_{0-4}-alkyl, aryl-C_{1-4}-heteroalkyl, heteroaryl-C_{0-4}-alkyl, C3-C6 cycloalkylaryl-C_{0-2}-alkyl are each optionally substituted with from one to three substituents independently selected from R1';

(b) R1', R26, R27, R28 and R31 are each independently selected from the group consisting of hydrogen, hydroxy, cyano, nitro, halo, oxo, C_1-C_6 alkyl, C_1-C_6 alkyl-COOR12, C_1-C_6 alkoxy, C_1-C_6 haloalkyl, C_1-C_6 haloalkyloxy, C_3-C_7 cycloalkyl, aryloxy, aryl-C_{0-4}-alkyl, heteroaryl, heterocycloalkyl, C(O)R13, COOR14, OC(O)R15, $OS(O)_2R16$, $N(R17)_2$, NR18C(O)R19, $NR20SO_2R21$, SR22, S(O)R23, $S(O)_2R24$, and

$S(O)_2N(R25)_2$; R12, R13, R14, R15, R16, R17, R18, R19, R20, R21, R22, R23, R24 and R25 are each independently selected from the group consisting of hydrogen, C_1-C_6 alkyl and aryl;

(c) R2 is selected from the group consisting of C_0-C_8 alkyl and C_{1-4}-heteroalkyl;

(d) X is selected from the group consisting of a single bond, O, S, $S(O)_2$ and N;

(e) U is an aliphatic linker wherein one carbon atom of the aliphatic linker is optionally replaced with O, NH or S, and wherein such aliphatic linker is optionally substituted with from one to four substituents each independently selected from R30;

(f) Y is selected from the group consisting of C, NH, and a single bond;

(g) E is C(R3)(R4)A or A and wherein

(i) A is selected from the group consisting of carboxyl, tetrazole, C_1-C_6 alkylnitrile, carboxamide, sulfonamide and acylsulfonamide; wherein sulfonamide, acylsulfonamide and tetrazole are each optionally substituted with from one to two groups independently selected from R^7;

(ii) each R^7 is independently selected from the group consisting of hydrogen, C_1-C_6 haloalkyl, aryl C_0-C_4 alkyl and C_1-C_6 alkyl;

(iii) R3 is selected from the group consisting of hydrogen, C_1-C_5 alkyl, and C_1-C_5 alkoxy; and

(iv) R4 is selected from the group consisting of H, C_1-C_5 alkyl, C_1-C_5 alkoxy, aryloxy, C_3-C_6 cycloalkyl, and aryl C_0-C_4 alkyl, and R3 and R4

are optionally combined to form a C_3-C_4 cycloalkyl, and wherein alkyl, alkoxy, aryloxy, cycloalkyl and aryl-alkyl are each optionally substituted with one to three substituents each independently selected from R26;

(h) B is selected from the group consisting of S, O, C, and N;

(i) Z is selected from the group consisting of N and C, with the proviso that when B is C then Z is N;

(j) R8 is selected from the group consisting of hydrogen, C_1-C_4 alkyl, C_1-C_4 alkylenyl, and halo;

(k) R9 is selected from the group consisting of hydrogen, C_1-C_4 alkyl, C_1-C_4 alkylenyl, halo, aryl-C_0-C_4 alkyl, heteroaryl, C_1-C_6 allyl, SR29, and OR29, and wherein aryl-C_0-C_4 alkyl, heteroaryl are each optionally substituted with from one to three independently selected from R27; R29 is selected from the group consisting of hydrogen, C_1-C_4 alkylenyl, and C_1-C_4 alkyl; R8 and R9 optionally combine to form a five membered fused bicyclic with the phenyl to which R8 and R9 attach, provided that when R8 and R9 form a fused ring, the group E-Y- is bonded at any available position on the five membered ring of such R8 and R9 fused bicyclic;

(l) R10, R11 are each independently selected from the group consisting of hydrogen, hydroxy, cyano, nitro, halo, oxo, C_1-C_6 alkyl, C_1-C_6 alkyl-COOR12'', C_0-C_6 alkoxy, C_1-C_6 haloalkyl, C_1-C_6. haloalkyloxy, C_3-C_7 cycloalkyl, aryl-C_{0-4}-alkyl, aryl- C_{1-4}-heteroalkyl, heteroaryl-C_{0-4}-alkyl, C3-C6 cycloalkylaryl-C_{0-2}-alkyl, aryloxy, C(O)R13',

COOR14', OC(O)R15', $OS(O)_2R16'$, $N(R17')_2$, NR18'C(O)R19', $NR20'SO_2R21'$, SR22', S(O)R23', $S(O)_2R24'$, and $S(O)_2N(R25')_2$; and wherein aryl-C_{0-4}-alkyl, aryl- C_{1-4}-heteroalkyl, heteroaryl-C_{0-4}-alkyl, and C3-C6 cycloalkylaryl-C_{0-2}-alkyl are each optionally substituted with from one to three substituents independently selected from R28;

(m) R12', R12'', R13', R14', R15', R16', R17', R18', R19', R20', R21', R22', R23', R24', and R25' are each independently selected from the group consisting of hydrogen, C_1-C_6 alkyl and aryl;

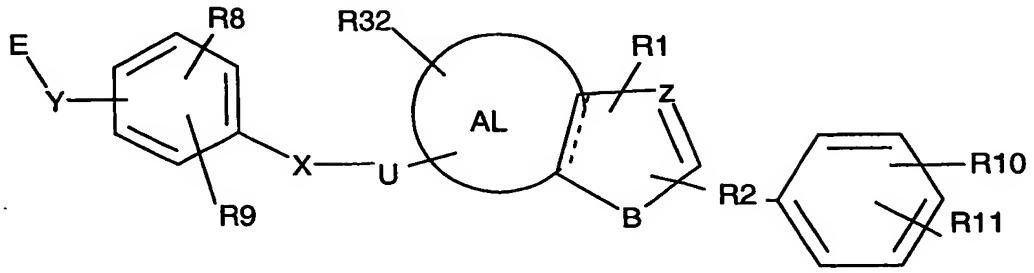
(n) R30 is selected from the group consisting of C_1-C_6 alkyl, aryl-C_{0-4}-alkyl, aryl- C_{1-4}-heteroalkyl, heteroaryl-C_{0-4}-alkyl, and C3-C6 cycloalkylaryl-C_{0-2}-alkyl, and wherein C_1-C_6 alkyl, aryl-C_{0-4}-alkyl, aryl- C_{1-4}-heteroalkyl, heteroaryl-C_{0-4}-alkyl, and C3-C6 cycloalkylaryl-C_{0-2}-alkyl are each optionally substituted with from one to three substituents each independently selected from R31;

(o) R32 is selected from the group consisting of a bond, hydrogen, halo, C_1-C_6 alkyl, C_1-C_6 haloalkyl, and C_1-C_6 alkyloxo;

(p) AL is selected from the group consisting of a fused C_3-C_8 carbocyclic, a fused pyridinyl, a fused pyrimidinyl, and a fused phenyl; and

(q) ---- is optionally a bond to form a double bond at the indicated position.

2. A compound of the structural Formula I'':



and stereoisomers, pharmaceutically acceptable salts, solvates and hydrates thereof, wherein:

(a) R1 is selected from the group consisting of hydrogen, C_1-C_8 alkyl, C_1-C_8 alkenyl, aryl-C_{0-4}-alkyl, aryl-C_{1-4}-heteroalkyl, heteroaryl-C_{0-4}-alkyl, C3-C6 cycloalkylaryl-C_{0-2}-alkyl, and, wherein C_1-C_8 alkyl, C_1-C_8 alkenyl, aryl-C_{0-4}-alkyl, aryl-C_{1-4}-heteroalkyl, heteroaryl-C_{0-4}-alkyl, C3-C6 cycloalkylaryl-C_{0-2}-alkyl are each optionally substituted with from one to three substituents independently selected from R1';

(b) R1', R26, R27, R28 and R31 are each independently selected from the group consisting of hydrogen, hydroxy, cyano, nitro, halo, oxo, C_1-C_6 alkyl, C_1-C_6 alkyl-COOR12, C_1-C_6 alkoxy, C_1-C_6 haloalkyl, C_1-C_6 haloalkyloxy, C_3-C_7 cycloalkyl, aryloxy, aryl-C_{0-4}-alkyl, heteroaryl, heterocycloalkyl, C(O)R13, COOR14, OC(O)R15, $OS(O)_2R16$, $N(R17)_2$, NR18C(O)R19, $NR20SO_2R21$, SR22, S(O)R23, $S(O)_2R24$, and $S(O)_2N(R25)_2$; R12, R13, R14, R15, R16, R17, R18, R19, R20, R21, R22, R23, R24 and R25 are each

independently selected from the group consisting of hydrogen, C_1-C_6 alkyl and aryl;

(c) R2 is selected from the group consisting of C_0-C_8 alkyl and C_{1-4}-heteroalkyl;

(d) X is selected from the group consisting of a single bond, O, S, $S(O)_2$ and N;

(b) U is an aliphatic linker wherein one carbon atom of the aliphatic linker is optionally replaced with O, NH or S, and wherein such aliphatic linker is substituted with from one to four substituents each independently selected from R30;

(e) Y is selected from the group consisting of C, O, S, NH and a single bond;

(f) E is C(R3)(R4)A or A and wherein

(i) A is selected from the group consisting of carboxyl, tetrazole, C_1-C_6 alkylnitrile, carboxamide, sulfonamide and acylsulfonamide; wherein sulfonamide, acylsulfonamide and tetrazole are each optionally substituted with from one to two groups independently selected from R^7;

(ii) each R^7 is independently selected from the group consisting of hydrogen, C_1-C_6 haloalkyl, aryl C_0-C_4 alkyl and C_1-C_6 alkyl;

(iii) R3 is selected from the group consisting of hydrogen, C_1-C_5 alkyl, and C_1-C_5 alkoxy; and

(iv) R4 is selected from the group consisting of H, C_1-C_5 alkyl, C_1-C_5 alkoxy, aryloxy, C_3-C_6 cycloalkyl, and aryl C_0-C_4 alkyl, and R3 and R4 are optionally combined to form a C_3-C_4 cycloalkyl, and wherein alkyl, alkoxy, aryloxy,

cycloalkyl and aryl-alkyl are each optionally substituted with one to three substituents each independently selected from R26;

(g) B is selected from the group consisting of S, O, C, and N;

(h) Z is selected from the group consisting of N and C; with the proviso that when B is C then Z is N;

(i) R8 is selected from the group consisting of hydrogen, C_1-C_4 alkyl, C_1-C_4 alkylenyl, and halo;

(j) R9 is selected from the group consisting of hydrogen, C_1-C_4 alkyl, C_1-C_4 alkylenyl, halo, aryl-C_0-C_4 alkyl, heteroaryl, C_1-C_6 allyl, SR29, and OR29, and wherein aryl-C_0-C_4 alkyl, heteroaryl are each optionally substituted with from one to three independently selected from R27; R29 is selected from the group consisting of hydrogen, C_1-C_4 alkylenyl, and C_1-C_4 alkyl; R8 and R9 optionally combine to form a five membered fused bicyclic with the phenyl to which R8 and R9 attach, provided that when R8 and R9 form a fused ring, the group E-Y- is bonded at any available position on the five membered ring of such R8 and R9 fused bicyclic;

(k) R10, R11 are each independently selected from the group consisting of hydrogen, hydroxy, cyano, nitro, halo, oxo, C_1-C_6 alkyl, C_1-C_6 alkyl-COOR12'', C_0-C_6 alkoxy, C_1-C_6 haloalkyl, C_1-C_6 haloalkyloxy, C_3-C_7 cycloalkyl, aryl-C_{0-4}-alkyl, aryl- C_{1-4}-heteroalkyl, heteroaryl-C_{0-4}-alkyl, C3-C6 cycloalkylaryl-C_{0-2}-alkyl, aryloxy, C(O)R13', COOR14', OC(O)R15', $OS(O)_2$R16', $N(R17')_2$, NR18'C(O)R19', NR20'SO_2R21', SR22', S(O)R23',

$S(O)_2R24'$, and $S(O)_2N(R25')_2$; and wherein aryl-C_{0-4}-alkyl, aryl- C_{1-4}-heteroalkyl, heteroaryl-C_{0-4}-alkyl, and C3-C6 cycloalkylaryl-C_{0-2}-alkyl are each optionally substituted with from one to three substituents independently selected from R28;

(l) R12', R12'', R13', R14', R15', R16', R17', R18', R19', R20', R21', R22', R23', R24', and R25' are each independently selected from the group consisting of hydrogen, C_1-C_6 alkyl and aryl;

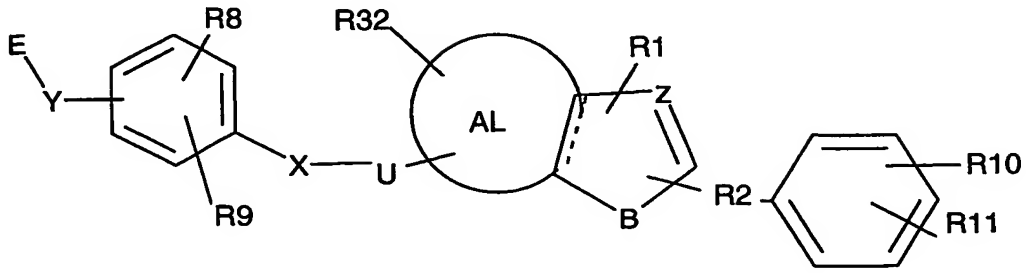
(m) R30 is selected from the group consisting of C_1-C_6 alkyl, aryl-C_{0-4}-alkyl, aryl- C_{1-4}-heteroalkyl, heteroaryl-C_{0-4}-alkyl, and C3-C6 cycloalkylaryl-C_{0-2}-alkyl, and wherein C_1-C_6 alkyl, aryl-C_{0-4}-alkyl, aryl- C_{1-4}-heteroalkyl, heteroaryl-C_{0-4}-alkyl, and C3-C6 cycloalkylaryl-C_{0-2}-alkyl are each optionally substituted with from one to three substituents each independently selected from R31;

(n) R32 is selected from the group consisting of a bond, hydrogen, halo, C_1-C_6 alkyl, C_1-C_6 haloalkyl, and C_1-C_6 alkyloxo;

(o) AL is selected from the group consisting of a fused C_3-C_8 carbocyclic, a fused pyridinyl, a fused pyrimidinyl, and a fused phenyl; and

(p) ---- is optionally a bond to form a double bond at the indicated position.

3. A compound of the structural Formula I''':



and stereoisomers, pharmaceutically acceptable salts, solvates and hydrates thereof, wherein:

(a) R1 is selected from the group consisting of hydrogen, C_1-C_8 alkyl, C_1-C_8 alkenyl, aryl-C_{0-4}-alkyl, aryl-C_{1-4}-heteroalkyl, heteroaryl-C_{0-4}-alkyl, C3-C6 cycloalkylaryl-C_{0-2}-alkyl, and, wherein C_1-C_8 alkyl, C_1-C_8 alkenyl, aryl-C_{0-4}-alkyl, aryl-C_{1-4}-heteroalkyl, heteroaryl-C_{0-4}-alkyl, C3-C6 cycloalkylaryl-C_{0-2}-alkyl are each optionally substituted with from one to three substituents independently selected from R1';

(b) R1', R26, R27, R28 and R31 are each independently selected from the group consisting of hydrogen, hydroxy, cyano, nitro, halo, oxo, C_1-C_6 alkyl, C_1-C_6 alkyl-COOR12, C_1-C_6 alkoxy, C_1-C_6 haloalkyl, C_1-C_6 haloalkyloxy, C_3-C_7 cycloalkyl, aryloxy, aryl-C_{0-4}-alkyl, heteroaryl, heterocycloalkyl, C(O)R13, COOR14, OC(O)R15, $OS(O)_2R16$, $N(R17)_2$, NR18C(O)R19, $NR20SO_2R21$, SR22, S(O)R23, $S(O)_2R24$, and $S(O)_2N(R25)_2$; R12, R13, R14, R15, R16, R17, R18, R19, R20, R21, R22, R23, R24 and R25 are each

independently selected from the group consisting of hydrogen, C_1-C_6 alkyl and aryl;

(c) R2 is selected from the group consisting of C_0-C_8 alkyl and C_{1-4}-heteroalkyl;

(d) X is selected from the group consisting of a single bond, O, S, $S(O)_2$ and N;

(e) U is an aliphatic linker wherein one carbon atom of the aliphatic linker is optionally replaced with O, NH or S, and wherein such aliphatic linker is optionally substituted with from one to four substituents each independently selected from R30;

(f) Y is selected from the group consisting of C, O, S, NH and a single bond;

(g) E is C(R3)(R4)A or A and wherein

(i) A is selected from the group consisting of carboxyl, tetrazole, C_1-C_6 alkylnitrile, carboxamide, sulfonamide and acylsulfonamide; wherein sulfonamide, acylsulfonamide and tetrazole are each optionally substituted with from one to two groups independently selected from R^7;

(ii) each R^7 is independently selected from the group consisting of hydrogen, C_1-C_6 haloalkyl, aryl C_0-C_4 alkyl and C_1-C_6 alkyl;

(iii) R3 is selected from the group consisting of hydrogen, C_1-C_5 alkyl, and C_1-C_5 alkoxy; and

(iv) R4 is selected from the group consisting of H, C_1-C_5 alkyl, C_1-C_5 alkoxy, aryloxy, C_3-C_6 cycloalkyl, and aryl C_0-C_4 alkyl, and R3 and R4 are optionally combined to form a C_3-C_4 cycloalkyl, and wherein alkyl, alkoxy, aryloxy,

cycloalkyl and aryl-alkyl are each optionally substituted with one to three substituents each independently selected from R26;

with the proviso that when Y is O then R4 is selected from the group consisting of C_1-C_5 alkyl, C_1-C_5 alkoxy, aryloxy, C_3-C_6 cycloalkyl, and aryl C_0-C_4 alkyl, and R3 and R4 are optionally combined to form a C_3-C_4 cycloalkyl, and wherein alkyl, alkoxy, cycloalkyl and aryl-alkyl are each optionally substituted with one to three each independently selected from R26;

(h) B is selected from the group consisting of S, O, C, and N;

(i) Z is selected from the group consisting of N and C; with the proviso that when B is C then Z is N;

(j) R8 is selected from the group consisting of hydrogen, C_1-C_4 alkyl, C_1-C_4 alkylenyl, and halo;

(k) R9 is selected from the group consisting of hydrogen, C_1-C_4 alkyl, C_1-C_4 alkylenyl, halo, aryl-C_0-C_4 alkyl, heteroaryl, C_1-C_6 allyl, SR29, and OR29, and wherein aryl-C_0-C_4 alkyl, heteroaryl are each optionally substituted with from one to three independently selected from R27; R29 is selected from the group consisting of hydrogen, C_1-C_4 alkylenyl, and C_1-C_4 alkyl; R8 and R9 optionally combine to form a five membered fused bicyclic with the phenyl to which R8 and R9 attach, provided that when R8 and R9 form a fused ring, the group E-Y- is bonded at any available position on the five membered ring of such R8 and R9 fused bicyclic;

(l) R10, R11 are each independently selected from the group consisting of hydrogen, hydroxy, cyano, nitro, halo, oxo, C_1-C_6 alkyl, C_1-C_6 alkyl-COOR12'', C_0-C_6 alkoxy, C_1-C_6 haloalkyl, C_1-C_6 haloalkyloxy, C_3-C_7 cycloalkyl, aryl-C_{0-4}-alkyl, aryl- C_{1-4}-heteroalkyl, heteroaryl-C_{0-4}-alkyl, C3-C6 cycloalkylaryl-C_{0-2}-alkyl, aryloxy, C(O)R13', COOR14', OC(O)R15', $OS(O)_2R16'$, $N(R17')_2$, NR18'C(O)R19', $NR20'SO_2R21'$, SR22', S(O)R23', $S(O)_2R24'$, and $S(O)_2N(R25')_2$; and wherein aryl-C_{0-4}-alkyl, aryl- C_{1-4}-heteroalkyl, heteroaryl-C_{0-4}-alkyl, and C3-C6 cycloalkylaryl-C_{0-2}-alkyl are each optionally substituted with from one to three substituents independently selected from R28;

(m) R12', R12'', R13', R14', R15', R16', R17', R18', R19', R20', R21', R22', R23', R24', and R25' are each independently selected from the group consisting of hydrogen, C_1-C_6 alkyl and aryl;

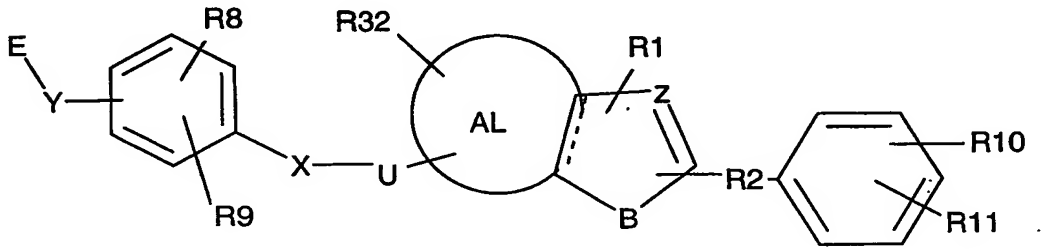
(n) R30 is selected from the group consisting of C_1-C_6 alkyl, aryl-C_{0-4}-alkyl, aryl- C_{1-4}-heteroalkyl, heteroaryl-C_{0-4}-alkyl, and C3-C6 cycloalkylaryl-C_{0-2}-alkyl, and wherein C_1-C_6 alkyl, aryl-C_{0-4}-alkyl, aryl- C_{1-4}-heteroalkyl, heteroaryl-C_{0-4}-alkyl, and C3-C6 cycloalkylaryl-C_{0-2}-alkyl are each optionally substituted with from one to three substituents each independently selected from R31;

(o) R32 is selected from the group consisting of a bond, hydrogen, halo, C_1-C_6 alkyl, C_1-C_6 haloalkyl, and C_1-C_6 alkyloxo;

(p) AL is selected from the group consisting of a fused C_3-C_8 carbocyclic, a fused pyridinyl, a fused pyrimidinyl, and a fused phenyl; and

(q) ---- is optionally a bond to form a double bond at the indicated position.

4. A compound of the Formula I:



and stereoisomers, pharmaceutically acceptable salts, solvates and hydrates thereof, wherein:

(a) R1 is selected from the group consisting of hydrogen, C_1-C_8 alkyl, C_1-C_8 alkenyl, aryl-C_{0-4}-alkyl, aryl-C_{1-4}-heteroalkyl, heteroaryl-C_{0-4}-alkyl, C3-C6 cycloalkylaryl-C_{0-2}-alkyl, and, wherein C_1-C_8 alkyl, C_1-C_8 alkenyl, aryl-C_{0-4}-alkyl, aryl-C_{1-4}-heteroalkyl, heteroaryl-C_{0-4}-alkyl, C3-C6 cycloalkylaryl-C_{0-2}-alkyl are each optionally substituted with from one to three substituents independently selected from R1';

(b) R1', R26, R27, R28 and R31 are each independently selected from the group consisting of hydrogen, hydroxy, cyano, nitro, halo, oxo, C_1-C_6 alkyl, C_1-C_6 alkyl-COOR12, C_1-C_6 alkoxy, C_1-C_6 haloalkyl, C_1-C_6 haloalkyloxy, C_3-C_7 cycloalkyl, aryloxy, aryl-C_{0-4}-alkyl, heteroaryl, heterocycloalkyl, C(O)R13, COOR14, OC(O)R15, $OS(O)_2R16$, $N(R17)_2$, NR18C(O)R19,

$NR20SO_2R21$, SR22, $S(O)R23$, $S(O)_2R24$, and $S(O)_2N(R25)_2$; R12, R13, R14, R15, R16, R17, R18, R19, R20, R21, R22, R23, R24 and R25 are each independently selected from the group consisting of hydrogen, C_1-C_6 alkyl and aryl;

(c) R2 is selected from the group consisting of C_0-C_8 alkyl and C_{1-4}-heteroalkyl;

(d) X is selected from the group consisting of a single bond, O, S, $S(O)_2$ and N;

(e) U is an aliphatic linker wherein one carbon atom of the aliphatic linker may be replaced with O, NH or S, and wherein such aliphatic linker is optionally substituted with R30;

(f) Y is selected from the group consisting of C, O, S, NH and a single bond;

(g) E is C(R3)(R4)A or A and wherein

(i) A is selected from the group consisting of carboxyl, tetrazole, C_1-C_6 alkylnitrile, carboxamide, sulfonamide and acylsulfonamide; wherein sulfonamide, acylsulfonamide and tetrazole are each optionally substituted with from one to two groups independently selected from R^7;

(ii) each R^7 is independently selected from the group consisting of hydrogen, C_1-C_6 haloalkyl, aryl C_0-C_4 alkyl and C_1-C_6 alkyl;

(iii) R3 is selected from the group consisting of hydrogen, C_1-C_5 alkyl, and C_1-C_5 alkoxy; and

(iv) R4 is selected from the group consisting of H, C_1-C_5 alkyl, C_1-C_5 alkoxy, aryloxy, C_3-C_6 cycloalkyl, and aryl C_0-C_4 alkyl, and R3 and R4

are optionally combined to form a C_3-C_4 cycloalkyl, and wherein alkyl, alkoxy, aryloxy, cycloalkyl and aryl-alkyl are each optionally substituted with one to three substituents each independently selected from R26;

(h) B is selected from the group consisting of S, O, C, and N, with the proviso that when B is N then Z is C;

(i) Z is selected from the group consisting of N and C; with the proviso that when B is C then Z is N;

(j) R8 is selected from the group consisting of hydrogen, C_1-C_4 alkyl, C_1-C_4 alkylenyl, and halo;

(k) R9 is selected from the group consisting of hydrogen, C_1-C_4 alkyl, C_1-C_4 alkylenyl, halo, aryl-C_0-C_4 alkyl, heteroaryl, C_1-C_6 allyl, and OR29, and wherein aryl-C_0-C_4 alkyl, heteroaryl are each optionally substituted with from one to three independently selected from R27; R29 is selected from the group consisting of hydrogen and C_1-C_4 alkyl;

(l) R10, R11 are each independently selected from the group consisting of hydrogen, hydroxy, cyano, nitro, halo, oxo, C_1-C_6 alkyl, C_1-C_6 alkyl-COOR12'', C_0-C_6 alkoxy, C_1-C_6 haloalkyl, C_1-C_6 haloalkyloxy, C_3-C_7 cycloalkyl, aryl-C_{0-4}-alkyl, aryl- C_{1-4}-heteroalkyl, heteroaryl-C_{0-4}-alkyl, C3-C6 cycloalkylaryl-C_{0-2}-alkyl, aryloxy, C(O)R13', COOR14', OC(O)R15', $OS(O)_2R16'$, $N(R17')_2$, NR18'C(O)R19', $NR20'SO_2R21'$, SR22', S(O)R23', $S(O)_2R24'$, and $S(O)_2N(R25')_2$; and wherein aryl-C_{0-4}-alkyl, aryl- C_{1-4}-heteroalkyl, heteroaryl-C_{0-4}-

alkyl, and C3-C6 cycloalkylaryl-C_{0-2}-alkyl are each optionally substituted with from one to three substituents independently selected from R28;

(m) R12', R12'', R13', R14', R15', R16', R17', R18', R19', R20', R21', R22', R23', R24', and R25' are each independently selected from the group consisting of hydrogen, C_1-C_6 alkyl and aryl;

(n) R30 is selected from the group consisting of C_1-C_6 alkyl, aryl-C_{0-4}-alkyl, aryl- C_{1-4}-heteroalkyl, heteroaryl-C_{0-4}-alkyl, and C3-C6 cycloalkylaryl-C_{0-2}-alkyl, and wherein C_1-C_6 alkyl, aryl-C_{0-4}-alkyl, aryl- C_{1-4}-heteroalkyl, heteroaryl-C_{0-4}-alkyl, and C3-C6 cycloalkylaryl-C_{0-2}-alkyl are each optionally substituted with from one to three substituents each independently selected from R31;

(o) R32 is selected from the group consisting of a bond, hydrogen, halo, C_1-C_6 alkyl, C_1-C_6 haloalkyl, and C_1-C_6 alkyloxo;

(p) AL is selected from the group consisting of a fused C_3-C_8 carbocyclic and a fused phenyl; and

(q) ---- is optionally a bond to form a double bond at the indicated position.

5. A compound as claimed by Claim 1 wherein X is -O-.

6. A compound as claimed by Claims 1 wherein X is -S.

7. A compound as claimed by any one of Claims 1 through 6 wherein Y is O.

8. A compound as claimed by any one of Claims 1 through 6 wherein Y is C.

9. A compound as claimed by any one of Claims 1 through 6 wherein wherein Y is S.

10. A compound as claimed by any one of Claims 1 through 9 wherein Z is N.

11. A compound as claimed by any one of Claims 1 through 9 wherein B is S or O.

12. A compound as claimed by any one of Claims 1 through 9, wherein B is N.

13. A compound as claimed by any one of Claims 1 through 9 wherein Z is N.

14. A compound as claimed by any one of Claims 1 through 13 wherein AL is a fused phenyl.

15. A compound as claimed by any one of Claims 1 through 13 wherein AL is a fused cycloalkyl.

16. A compound as claimed by any one of Claims 1 through 13 wherein AL is a fused pyrimidinyl.

17. A compound as claimed by any one of Claims 1 through 13 wherein AL is a fused pyridinyl.

18. A compound as claimed by any one of Claims 1 through 13 or Claim 15 wherein ---- is a bond to form a double bond at the designated location on Formula I.

19. A compound as claimed by any one of Claims 1 through 18 wherein E is C(R3)(R4)A.

20. A compound as claimed by any one of Claims 1 through 18 wherein E is A.

21. A compound as claimed by any one of Claims 1 through 19 wherein A is COOH.

22. A compound as claimed by any one of Claims 1 through 21 wherein R10 is haloalkyl.

23. A compound as claimed by any one of Claims 1 through 22 wherein R10 is CF_3.

24. A compound as claimed by any one of Claims 1 through 21 wherein R10 is haloalkyloxy.

25. A compound as claimed by any one of Claims 1 through 21 wherein R10 and R11 are each independently selected from the group consisting of hydrogen, halo, oxo, C_1-C_6 alkyl, C_1-C_6 alkyl-COOR12'', C_1-C_6 alkoxy, C_1-C_6 haloalkyl, and C_1-C_6 haloalkyloxy.

26. A compound as claimed by any one of Claims 1 through 21 wherein R10 is selected from the group consisting of C_3-C_7 cycloalkyl, aryl-C_{0-4}-alkyl, aryl-C_{1-4}-heteroalkyl, heteroaryl-C_{0-4}-alkyl, C3-C6 cycloalkylaryl-C_{0-2}-alkyl, and aryloxy.

27. A compound as claimed by any one of Claims 1 through 26 wherein R8 is selected from the group consisting of C_1-C_3 alkyl and C_1-C_4 alkylenyl.

28. A compound as claimed by any one of Claims 1 through 26, wherein R8 and R9 are each independently selected from the group consisting of hydrogen and C_1-C_3 alkyl.

29. A compound as claimed by any one of Claims 1 through 27 wherein R29 is C_1-C_4 alkylenyl.

30. A compound as claimed by any one of Claims 1 through 27 and 29 wherein R8 is C_1-C_4 alkylenyl.

31. A compound as claimed by any one of Claims 1 through 27, 29, and 30 wherein R9 is OR29.

32. A compound as claimed by any one of Claims 1 through 27, 29, and 30 wherein R9 is SR29.

33. A compound as claimed by any one of Claims 1 through 27, 29 through 32 wherein R8 and R9 combine to form a fused bicyclic.

34. A compound as claimed by any one of Claims 1 through 33 wherein R1, R2, R3, and R4 are each

independently selected from the group consisting of C_1-C_2 alkyl.

35. A compound as claimed by any one of Claims 1 through 33 wherein R1, R3, and R4 are each independently selected from the group consisting of hydrogen and C_1-C_2 alkyl.

36. A compound as claimed by any one of Claims 1 through 33 and 35 wherein R2 is a bond.

37. A compound as claimed by any one of Claims 1 through 36 wherein U is C_1-C_3 alkyl.

38. A compound as claimed by Claim 37 wherein U is saturated.

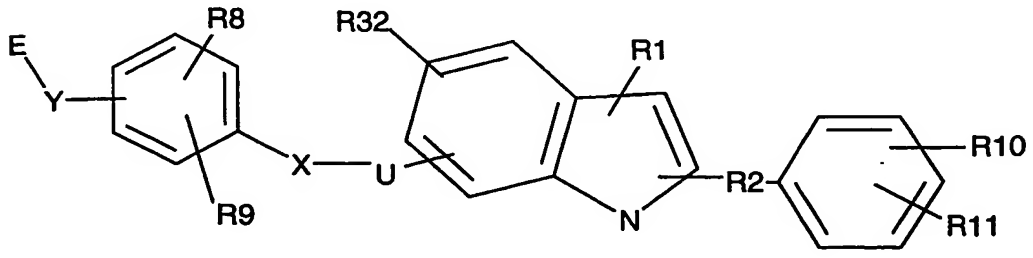
39. A compound as claimed by any one of Claims 37 or 38 wherein U is substituted with C_1-C_3 alkyl.

40. A compound as claimed by any one of Claims 1 through 39 wherein aliphatic linker is substituted with from one to four substituents each independently selected from the group consisting of R30.

41. A compound as claimed by any one of Claims 1 through 38, 39, and 40 wherein one carbon of the aliphatic linker is replaced with an -O-.

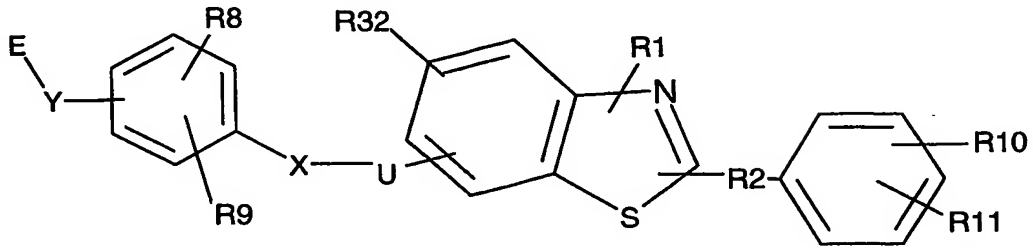
42. A compound as claimed by any one of Claims 1 through 9, 12, 13, 14, Claims 18 through 32, Claims 34 through 41 of the Structural Formula

II



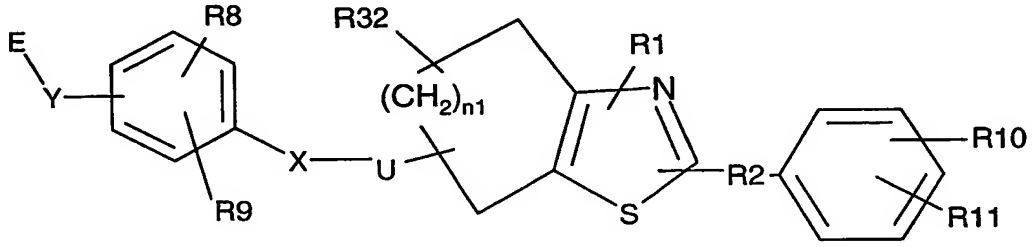
43. A compound as claimed by any one of Claims 1 through 11, 13, 14, Claims 17 through 32, Claims 34 through 41 of the Structural Formula

III:



44. A compound as claimed by any one of Claims 1 through 11, 15, Claims 18 through 32, Claims 34 through 41 of the Structural Formula

IV:

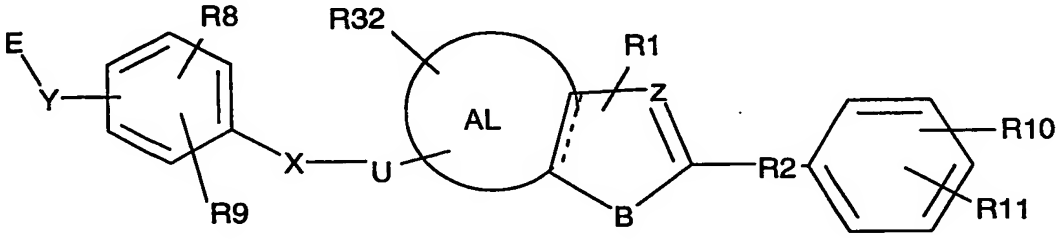


;

wherein n1 is 1 to 5.

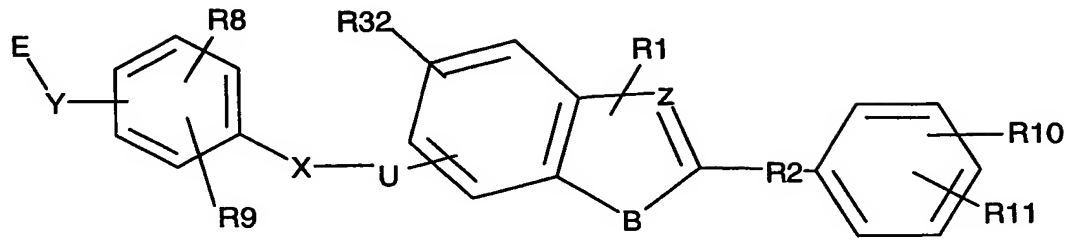
45. A compound as claimed by any one of Claims 1 through 14, 18 through 32, Claims 34 through 41 of the Structural Formula

V:

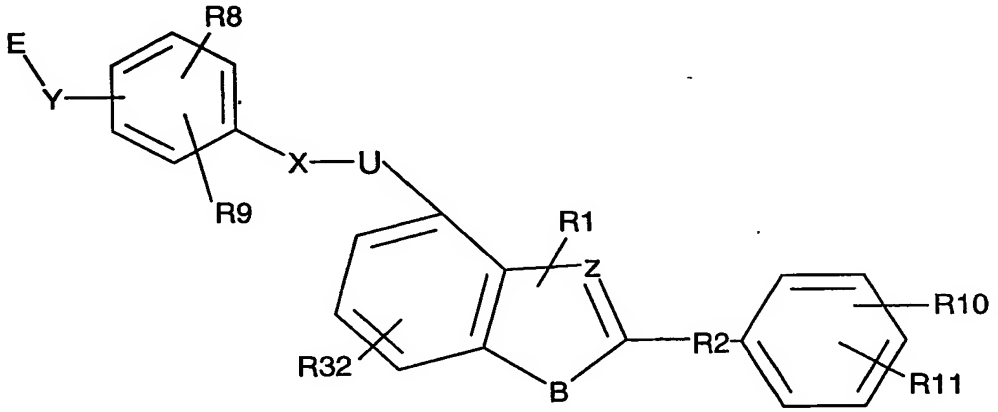


46. A compound as claimed by any one of Claims 1 through 14, Claims 18 through 32 Claims 34 through 41

of the Structural Formula VI:



47. A compound as claimed by any one of Claims 1 through 14, Claims 18 through 32, Claims 34 through 41 of the Structural Formula VII:

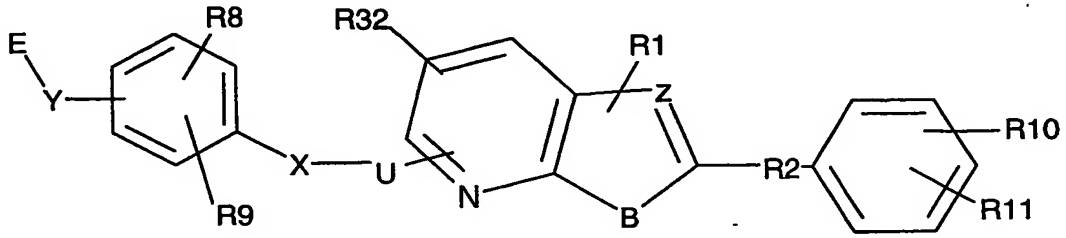


48. A compound as claimed by any one of Claims 1 through 14, Claims 18 through 32, Claims 34 through 47 wherein X is S, Y is selected from the group consisting of C and O, E is CH_2COOH, and R2 is a bond.

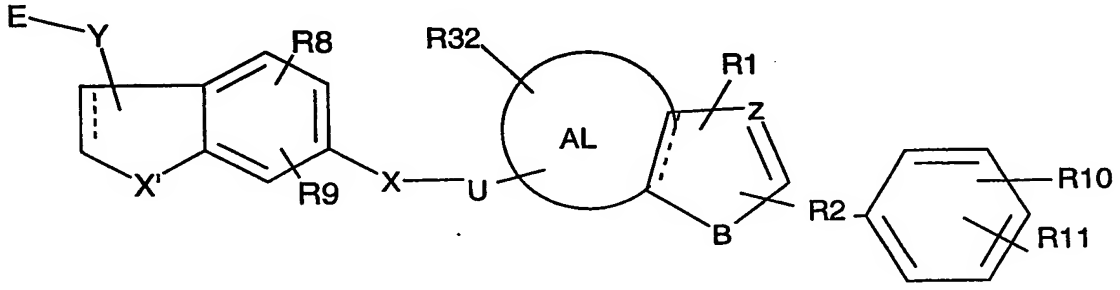
49. A compound as claimed by any one of Claims 1 through 11, and Claims 13 through 48, wherein Z is N and B is S.

50. A compound as claimed by any one of Claims 1 through 49 wherein R32 is hydrogen, R8 is hydrogen and R9 is C_1-C_4 alkyl.

51. A compound as claimed by any one of Claims 1 through 13, 17, Claims 18 through 32, Claims 34 through 41 of the Structural Formula VIII:

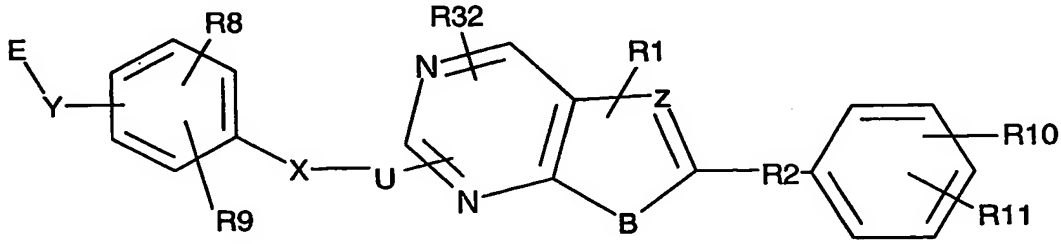


52. A compound as claimed by any one of Claims 1 through through 32 Claims 34 through 41 of the Structural Formula IX:



wherein X' is selected from the group consisting of O and S.

53. A compound as claimed by any one of Claims 1 through 13, 16, Claims 18 through 32 Claims 34 through 41 of the Structural Formula X:



54. A compound as claimed by any one of Claims 1 through 4 wherein the compound is selected from the group consisting of

Racemic-{2-Methyl-4-[2-(4-trifluoromethyl-phenyl)-5,6-dihydro-4H-cyclopentathiazol-4-ylmethylsulfanyl]-phenoxy}-acetic acid;

(R)-{2-Methyl-4-[2-(4-trifluoromethyl-phenyl)-5,6-dihydro-4H-cyclopentathiazol-4-ylmethylsulfanyl]-phenoxy}-acetic acid;

(S)-{2-Methyl-4-[2-(4-trifluoromethyl-phenyl)-5,6-dihydro-4H-cyclopentathiazol-4-ylmethylsulfanyl]-phenoxy}-acetic acid;

Racemic-3-{2-Methyl-4-[2-(4-trifluoromethyl-phenyl)-5,6-dihydro-4H-cyclopentathiazol-4-ylmethoxy]-phenyl}-propionic acid;

Racemic-3-{2-Methyl-4-[2-(4-trifluoromethyl-phenyl)-5,6-dihydro-4H-cyclopentathiazol-4-ylmethylsulfanyl]-phenyl}-propionic acid;

(R)-3-{2-Methyl-4-[2-(4-trifluoromethyl-phenyl)-5,6-dihydro-4H-cyclopentathiazol-4-ylmethylsulfanyl]-phenyl}-propionic acid;

(S)-3-{2-Methyl-4-[2-(4-trifluoromethyl-phenyl)-5,6-dihydro-4H-cyclopentathiazol-4-ylmethylsulfanyl]-phenyl}-propionic acid;

Racemic-{2-Methyl-4-[2-(4-trifluoromethyl-phenyl)-4,5,6,7-tetrahydro-benzothiazol-4-ylmethylsulfanyl]-phenoxy}-acetic acid;

(S)-{2-Methyl-4-[2-(4-trifluoromethyl-phenyl)-4,5,6,7-tetrahydro-benzothiazol-4-ylmethylsulfanyl]-phenoxy}-acetic acid;

(R)-{2-Methyl-4-[2-(4-trifluoromethyl-phenyl)-4,5,6,7-tetrahydro-benzothiazol-4-ylmethylsulfanyl]-phenoxy}-acetic acid;

{2-Methyl-4-[2-(4-trifluoromethyl-phenyl)-4,5,6,7-tetrahydro-benzothiazol-4-ylmethoxy]-phenoxy}-acetic acid;

Racemic-3-{2-Methyl-4-[2-(4-trifluoromethyl-phenyl)-4,5,6,7-tetrahydro-benzothiazol-4-ylmethylsulfanyl]-phenyl}-propionic acid;

(R)-3-{2-Methyl-4-[2-(4-trifluoromethyl-phenyl)-4,5,6,7-tetrahydro-benzothiazol-4-ylmethylsulfanyl]-phenyl}-propionic acid;

(S)-3-{2-Methyl-4-[2-(4-trifluoromethyl-phenyl)-4,5,6,7-tetrahydro-benzothiazol-4-ylmethylsulfanyl]-phenyl}-propionic acid;

{3-[2-(4-Trifluoromethyl-phenyl)-5,6-dihydro-4H-cyclopentathiazol-4-ylmethoxy]-phenyl}-acetic acid;

(S)-{3-[2-(4-Trifluoromethyl-phenyl)-5,6-dihydro-4H-cyclopentathiazol-4-ylmethoxy]-phenyl}-acetic acid;

(R)-{3-[2-(4-Trifluoromethyl-phenyl)-5,6-dihydro-4H-cyclopentathiazol-4-ylmethoxy]-phenyl}-acetic acid;

{2-Methyl-4-[7-methyl-2-(4-trifluoromethyl-phenyl)-4,5,6,7-tetrahydro-benzothiazol-4-ylmethylsulfanyl]-phenoxy}-acetic acid;

(S)-3-{2-Methyl-4-[2-(4-trifluoromethyl-phenyl)-4,5,6,7-tetrahydro-benzothiazol-4-ylmethoxy]-phenyl}-propionic acid;

(R)-3-{2-Methyl-4-[2-(4-trifluoromethyl-phenyl)-4,5,6,7-tetrahydro-benzothiazol-4-ylmethoxy]-phenyl}-propionic acid;

(R)-{3-[2-(4-Trifluoromethyl-phenyl)-4,5,6,7-tetrahydro-benzothiazol-4-ylmethoxy]-phenyl}-acetic acid;

(S)-{3-[2-(4-Trifluoromethyl-phenyl)-4,5,6,7-tetrahydro-benzothiazol-4-ylmethoxy]-phenyl}-acetic acid;

3-{2-Methyl-4-[2-(4-trifluoromethyl-phenyl)-5,6,7,8-tetrahydro-4H-cycloheptathiazol-4-ylmethylsulfanyl]-phenyl}-propionic acid;

{2-Methyl-4-[2-(4-trifluoromethyl-phenyl)-5,6,7,8-tetrahydro-4H-cycloheptathiazol-4-ylmethylsulfanyl]-phenoxy}-acetic acid;

(R)-{2-Methyl-4-[2-(4-trifluoromethyl-phenyl)-5,6,7,8-tetrahydro-4H-cycloheptathiazol-4-ylmethylsulfanyl]-phenoxy}-acetic acid;

(S)-{2-Methyl-4-[2-(4-trifluoromethyl-phenyl)-5,6,7,8-tetrahydro-4H-cycloheptathiazol-4-ylmethylsulfanyl]-phenoxy}-acetic acid;

3-{2-Methyl-4-[2-(4-trifluoromethyl-phenyl)-5,6,7,8-tetrahydro-4H-cycloheptathiazol-4-ylmethoxy]-phenyl}-propionic acid;

{3-[2-(4-Trifluoromethyl-phenyl)-5,6,7,8-tetrahydro-4H-cycloheptathiazol-4-ylmethoxy]-phenyl}-acetic acid;

(R)-3-{2-Methyl-4-[2-(4-trifluoromethyl-phenyl)-5,6,7,8-tetrahydro-4H-cycloheptathiazol-4-ylmethylsulfanyl]-phenyl}-propionic acid;

(S)-3-{2-Methyl-4-[2-(4-trifluoromethyl-phenyl)-5,6,7,8-tetrahydro-4H-cycloheptathiazol-4-ylmethylsulfanyl]-phenyl}-propionic acid;

{2-Methyl-4-[2-(4-trifluoromethyl-phenyl)-4,5,6,7,8,9-hexahydro-cyclooctathiazol-4-ylmethylsulfanyl]-phenoxy}-acetic acid;

{2-Methyl-4-[2-(4-trifluoromethyl-phenyl)-benzothiazol-4-ylmethylsulfanyl]-phenoxy}-acetic acid;

{2-Methyl-4-[2-(4-trifluoromethyl-phenyl)-benzothiazol-4-ylmethylsulfanyl]-phenoxy}-acetic acid ethyl ester;

3-{2-Methyl-4-[2-(4-trifluoromethyl-phenyl)-benzothiazol-4-ylmethylsulfanyl]-phenyl}-propionic acid;

{3-[2-(4-Trifluoromethyl-phenyl)-benzothiazol-4-ylmethoxy]-phenyl}-acetic acid;

3-{2-Methyl-4-[2-(4-trifluoromethyl-phenyl)-benzothiazol-4-ylmethoxy]-phenyl}-propionic acid;

(S)-2-Methoxy-3-{4-[2-(4-trifluoromethyl-phenyl)-benzothiazol-4-ylmethoxy]-phenyl}-propionic acid;

2-Methyl-2-{2-methyl-4-[2-(4-trifluoromethyl-phenyl)-benzothiazol-4-ylmethoxy]-phenoxy}-propionic acid;

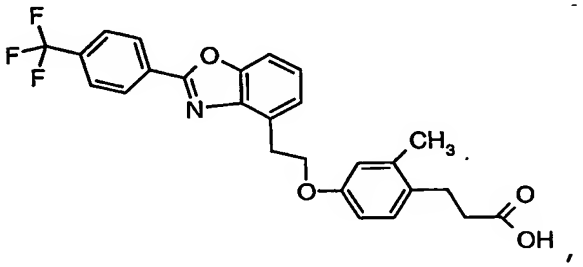
Racemic-(2-methyl-4-{1-[2-(4-trifluoromethyl-phenyl)-benzothiazol-4-yl]-ethylsulfanyl}-phenoxy)-acetic acid; and

Racemic-3-(2-methyl-4-{1-[2-(4-trifluoromethyl-phenyl)-benzothiazol-4-yl]-ethylsulfanyl}-phenyl)-propionic acid.

55. A compound as claimed by any one of Claims 1 through 4 which is selected from the group consisting of {2-Methyl-4-[2-(4-trifluoromethyl-phenyl)-benzothiazol-4-ylmethylsulfanyl]-phenoxy}-acetic acid and 3-{2-Methyl-4-[2-(4-trifluoromethyl-phenyl)-benzothiazol-4-ylmethylsulfanyl]-phenyl}-propionic acid.

56. A compound as claimed by any one of Claims 1 through 4 selected from the group consisting of

2-Ethyl-4-[2-(4-trifluoromethylphenyl)benzothiazol-4-ylmethylsulfanylphenoxyacetic Acid; 3-[2-(4-Trifluoromethylphenyl)benzothiazol-4-ylmethylsulfanyl-phenylacetic Acid; 6-[2-(4-Trifluoromethylphenyl)benzothiazol-4-ylmethylsulfanyl]benzo[*b*]thiophen-3-yl}acetic Acid; 2-Ethyl-4-[2-(4-trifluoromethylphenyl)benzothiazol-7-ylmethylsulfanyl]phenoxyacetic Acid; and 2-Ethyl-4-[2-(4-trifluoromethylphenyl)-3*H*-imidazo[4,5-*b*]pyridin-7-ylmethylsulfanyl]phenoxyacetic Acid,



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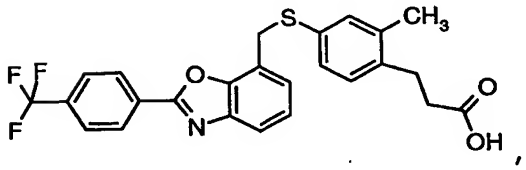

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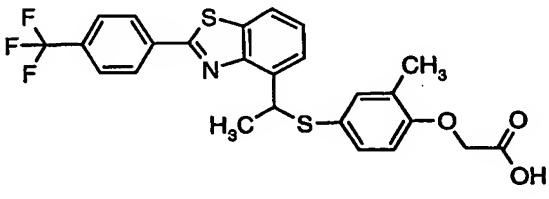
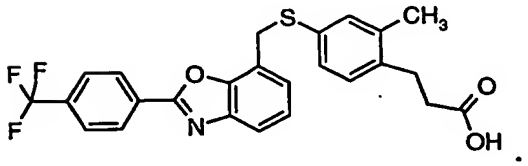


, and



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57. A compound as claimed by any one of Claims 1 through 55 that is in the S conformation.

58. A compound as claimed by any one of Claims 1 through 55 that is in the R conformation.

59. A pharmaceutical composition, comprising as an active ingredient, at least one compound as claimed by any one of Claims 1 through 58 together with a pharmaceutically acceptable carrier or diluent.

60. A method of modulating a peroxisome proliferator activated receptor, comprising the step of contacting the receptor with at least one compound as claimed by any one of Claims 1 through 58.

61. A method of treating diabetes mellitus in a mammal, comprising the step of administering to the mammal in need thereof a therapeutically effective amount of at least one compound of Claims 1 through 58.

62. A method of treating Metabolic Syndrome in a mammal, comprising the step of administering to the mammal in need thereof a therapeutically effective amount of at least one compound of Claims 1 through 58.

63. A method of selectively modulating a PPAR delta receptor comprising administering a compound as claimed by any one of Claims 1 through 58 to a mammal in need thereof.

64. The manufacture of a medicament for use in the treatment and/or prevention of a condition mediated by nuclear receptors, in particular by a peroxisome proliferator activated receptor, wherein the compound is a compound as claimed by any one of Claims 1 through 58.

65. A method for treating or preventing the progression of cardiovascular disease in a mammal in need thereof comprising administering a therapeutically effective amount of a compound as Claimed by any one of Claims 1 through 58.

66. A method as claimed by Claim 65 wherein the mammal is diagnosed as being in need of such treatment.

67. A method of treating arthritis in a mammal, comprising the step of administering to the mammal in need thereof, a therapeutically effective amount of at least one compound as claimed by any one of Claims 1 through 58.

68. A method of treating demyelating disease in a mammal, comprising the step of administering to the mammal in need thereof, a therapeutically effective amount of at least one compound as claimed by any one of Claims 1 through 58.

69. A method of treating inflammatory disease in a mammal, comprising the step of administering to the mammal in need thereof, a therapeutically effective amount of at least one compound as claimed by any one of Claims 1 through 58.

70. A method as claimed by any one of Claims 67, 68, and 69 wherein such mammal is diagnosed as being in need of such treatment.

71. A compound as Claimed by any one of Claims 1 through 58 for use as a pharmaceutical.

72. A compound as claimed by any one of Claims 1 through 58 wherein the compound is radiolabeled.

73. A compound as disclosed by any one of the Examples herein.

74. All methods disclosed herein of preparing the compounds as claimed by any one of Claims 1 through 4.